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Investigation and analysis of clinical trial research nurse to perform standard operating procedures

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ABSTRACT

Objective: The aim of this study was to investigate the situations and factors that cause nurses not to follow standard operating procedures (SOPs) during the clinical trial process.
Methods: Five cases involving patients enrolled in a clinical trial were divided into two groups, pre-SOP training and post-SOP training, to compare and observe the process problems and whether nurses followed SOPs in clinical trials. The causes of problems were analyzed and corrective measures were proposed.
Results: Our results indicate significant improvement in compliance with SOPs after training. There were three occurrences of irregular behavior after training compared with 21 occurrences of irregular behavior before training.
Conclusions: The quality of clinical trials can be improved if nurses strictly follow SOPs.

1. Introduction

Standard operating procedures (SOPs) are developed to establish written standards and detailed protocols in each work environment and operation to ensure accurate completion of clinical trials. This study was a randomized, controlled clinical trial; the test drug and control drug had the same dosage, appearance, color, and taste. Researchers and participants did not know if the drug used by the subject was the test drug or the control drug.[1] This double-blind approach avoids assessment bias (the tendency to favor new therapies) and possible psychological effects in subjects. If subjects know that they are using the test drug or the control, their attitudes, their cooperation, and their answers to treatment questions can be affected. Double-blind trials ensure assessment efficacy, adverse reactions are stated more objectively, and the test is more scientifically valid. The first topic in Good Clinical Practice (GCP) training involves quality assurance, which stresses the need to adopt SOPs to ensure the implementation of quality control and quality assurance systems in clinical trials.[2] Therefore, it is important to strictly enforce SOPs in clinical trials to ensure the quality of drug clinical trials.

2. Methods

2.1. Clinical data

From May 2013 to October 2014, three clinical trial programs with 55 cases were evaluated. The inclusion criteria are as follows. The clinical trial cases were randomized control trials that included infusion and oral intake. The 55 clinical trial cases were divided into pre-SOP and post-SOP training groups, containing 27 and 28 cases, respectively. Pre-SOP and post-SOP training activities were compared for 9 research nurses. There was no statistical significance in the general information of the two groups ($P > 0.05$), which were comparable.

2.2. Methods

In the pre-SOP training group, the research nurses had standard GCP training but not systematic SOP training. In the post-SOP training group, the research nurses had standard GCP training and systematic SOP training. The following aspects were carefully observed: implementation of the standards of medicine

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administration by the nurse, whether the research nurse talked about clinical trial–relevant information, file storage, drug recovery, and comparison of activities before and after training. Data processing was done using IBM SPSS version 13.3 statistical software. $P < 0.05$ was considered statistically significant.

3. Results

The quality after training was significantly higher than the quality before training (Tables 1 and 2).

4. Strategies

4.1. All health-care workers participating in this clinical trial must have a rigorous scientific attitude

Workers must realize that they cannot disclose information concerning random number generation, test drug coding, subject number, test group, experimental results and evaluation, or data management.

4.2. Standardization of job duties is a basic requirement of clinical trials

Before the test starts, research nurses must attend a research project discussion to become familiar with the clinical trial program.[3] Adequate preparation before the trial is required for successful trial completion.

4.3. There will be someone specifically responsible for the drugs, which must be kept in a locked location

There will be designated store counters for clinical trial drugs and drugs will be regularly inventoried. The time of drug removal and administration must be recorded and signed. Empty drug bottles and any remaining drugs shall not be discarded.[4]

4.4. Documents

After the establishment of the SOP file, responsibilities of different staff are clarified and standard operations are collected to ensure the quality of data; even if no error occurs, there will be documents to check.[5] The operating procedures must be further improved during clinical implementation process to guarantee that the SOPs are always up to date. If it is a double-blind trial, during the entire trial process, nurses will be divided into single- and double-blinded groups for their duties. Nurses in the single-blind group should have a separate working place; must keep their information confidential; cannot randomly discuss specific circumstances of the trial drug with doctors, nurses, or other participants; and the file must be separately saved. Nurses in the double-blind group must remain cautious in this process and be ready to accept inspection by supervisory staff.[6]

Table 1
Assessment of problems in operating procedures conducted by research nurse.

Violation of operating	Before training (occurrences)	After training (occurrences)
Drug recovery	8	2
Talking about clinical trial-relevant information	2	0
File storage	6	1
Unlocked location	5	0
Total	21	3

Note: Comparison of the two groups ($P < 0.05$).

Table 2
Factors affecting the double-blind trial status.

Factors	Number of nurses
Attitude is not rigorous	3
Not familiar with SOPs	2
SOPs imperfect	8
Not familiar with the program	3

4.5. The duties and practices of research nurses in a trial test

4.5.1. Double-blind nurse duties

A rigorous testing process must be based on a professional work style, scientific management methods, and a scientific and realistic attitude toward subjects under nurse management. (1) Before establishing the group, nurses must be proficient in trial-relevant knowledge, implementing participant recruitment, assisting participants in fully understanding the trial and agreeing with it, and must use language that allows participants and families to fully and accurately understand the details of the clinical trial. Through good communication, participants will decide whether to sign the clinical trial agreement.[7] When participants completely understand and volunteer to participate in a trial, attention must be paid to psychologically building mutual trust between the nurse and the participant to improve trial compliance. (2) Research nurses must administer medicine strictly according to the SOP trial implementation program. Before following the doctor's prescription, nurses must repeatedly read treatment programs to further understand relevant information about the trial drug, such as the dosage of oral medication, medication time, frequency, injection drug formula, infusion rate, number of drugs, and whether fits “five taboo”. It is important to strictly implement “three- and seven-checks”, aseptic principles, and ensure the medication standard. (3) The observation of trial drug–relevant adverse reactions and emergency treatment measures must be controlled. While using the drug, the process should be thoroughly inspected. Nurses must have good communication with participants and closely observe each subject's vital signs. When any event occurs during the test, nurses must closely observe the reaction after medicine administration. Detailed information about the event must be recorded to assist in instantly detecting future adverse events, ensure the safety of subjects, and to avoid serious consequences. The researcher can decide whether to open the blind to subjects depending on the circumstances. Research nurses cannot decide to lift the blind by themselves. After training, the quality of the blind clinical trial significantly improves.[8]

4.5.2. Duties of nurses lifting the blind

(1) Nurses are responsible for receiving and storing drugs. Management principles include management by a specific person, designed locks, specific counters, special refrigerators, special account records, and maintenance of a daily record of humidity and refrigerator temperature. (2) Unblinded nurses call the interactive voice response (IVR) system and receive grouping information for test subjects. The nurse saves the record of participant test distribution and places the record in the specific folder to avoid breaches. (3) Drugs must be distributed according to the drug program and drug number. The outside of the box must show the nurse's initials, number, and medicine administration time; all information will be carefully checked and the drug distribution completed. The drug liquid should be prepared in a separate treatment room and others are prohibited from entering when dispensing. To prevent

revealing whether the subject is in the experimental or control group based on the color of the liquid, the drug should be packaged in a dark bag while preparing, and dark infusion should be used to maintain blindness. (4) The name of the drug on the label that is attached to the infusion bag should be uniform, regardless of whether it contains the experimental or the control drug.[9] (5) After dispensing is finished, research nurses must carefully check and carefully count the number of drugs, record the information, and register the remaining drug and the empty box. Due to the special nature of the test drug, the empty bottles, medicine bags, and remaining medicines cannot be randomly discarded after use; they must be gathered and recycled. At the end of the trial, all materials must be recycled by a clinical pharmacologic agency; they cannot be mixed with other medical waste. (6) According to the dispensing time and frequency interval, the drug must be placed in a particular environment and will be used within the validity period. (7) Immediately fill the drug-prescribing form, accurately record the dispensing time, and sign the form.[10] If there is any concern, contact the unblinded inspector directly. Unblinded nurses should avoid any direct contact with participants.

5. Discussion

Through the above observation during clinical trial procedures, we found that the personal responsibility of research nurses required some adjustment. Research nurses might violate sections of work in the clinical trial SOP, such as revealing blinded information to unblinded staff while charting. Individual research nurses might think that they can assist in the completion of a clinical trial task, and that they do not need to be familiar with or fully understand the test program. This situation can result in failure to handle all details according to the correct procedures during implementation. In a double-blind trial, effort must be made to maintain blindness. Health-care workers who are involved in research or subject management should not ask about or know if a participant is in the test or control group, and must not reveal the identity of the research nurse who knows the random results or any other relevant information to subjects and their families. Effort must be made to prevent events that result from blind-trial information leaks to avoid bias caused by human factors. Only through training and enhanced cautious behavior by research nurses, strengthening nursing research awareness, and broadening the nurses' understanding of clinical trials, can one avoid affecting the objectivity of the test results.

If SOPs are not strictly followed, research nurses can face operational difficulties and the blind aspect of the clinical trial can be compromised. By following consistent standard-of-care procedures, formulating a manageable workflow, and establishing a clinical practice routine, the implementation capacity of research nurses will be improved and human error in clinical trials will be minimized.

Research nurses who participate in new drug trials must participate in drug GCP training and become familiar with all standard test regulations to strengthen training and improve quality. Research nurses require research thinking and consciousness, and must be competent in finding problems in clinical practice, finding ways to resolve those problems, and organically combining clinical practice and clinical trials to improve clinical trial quality. In clinical trial, it was possible to instantly identify problems, take effective measures, and strengthen research nurses' professional knowledge and skills training, and to provide training on vocational ethics and scientific attitudes.

Clinical trials in China are increasing due to the globalization of drug development, and the number of international clinical trial centers in China has grown in recent years. The level of our clinical trials has gradually gained international recognition. However, there is a shortage of research resources in our medical institutions and there is no mature clinical trial project management system. Because research nurses are involved in clinical trials, they must focus on learning the basic methods of scientific research and establishing complete nurse management methods in individual tests to ensure that clinical trials are conducted smoothly.

Conflicts of interest

The contributing authors have no conflicts of interest to declare.

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